UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/787,421	02/26/2004	Majed M. Hamawy	960296.99187	5432

27114 7590 08/13/2007
QUARLES & BRADY LLP
411 E. WISCONSIN AVENUE, SUITE 2040
MILWAUKEE, WI 53202-4497

EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	**PAPER NUMBER**
1644	

NOTIFICATION DATE	DELIVERY MODE
08/13/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

pat-dept@quarles.com

Office Action Summary	Application No.	Applicant(s)	
	10/787,421	HAMAWY, MAJED M.	
	Examiner	Art Unit	
	Nora M. Rooney	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,9 and 14-17* is/are pending in the application.

4a) Of the above claim(s) *14-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 9 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed on 07/23/2007 is acknowledged.

2. Claims 2, 9 and 14-17 are pending.

3. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/23/2007 has been entered.

4. Claims 14-16 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/02/2006.

5. Claims 2, 9 and 17 are currently under examination as they read on a method for monitoring whether an animal is experiencing kidney transplant rejection by detecting the protein of SEQ ID NO:1 in a kidney tissue sample.

6. The following new grounds of rejection are necessitated by the amendments filed on 07/23/2007

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 2, 9 and 17 and rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17, lines 11-14 and all claims dependent thereupon recite that the marker protein can be detected in the kidney sample and that a fragment of the marker protein can be detected in the homogenate of the kidney sample. It is unclear why the marker protein cannot be detected in the kidney sample homogenate. It is also unclear why the kidney sample homogenate contains fragments of the marker protein.

Claim 17, lines 7-8 and all claims dependent thereupon recites that the phosphorylated protein of SEQ ID NO:1 can be detected by the method. It is unclear how an antibody to SEQ ID NO:1 is able to detect a phosphorylated protein since the specificity of the antibody is for SEQ ID NO:1, not phosphorylated SEQ ID NO:1.

9. Claims 2, 9 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are a contact step and a resolution step: it is unclear how to analyze the sample for the presence of phosphorylated SEQ ID NO:1 using antibodies to SEQ ID NO:1. The claimed method cannot be performed by the recited steps because no method of detecting phosphorylation levels is recited. It is also unclear how detecting phosphorylated SEQ ID NO:1 relates to a whether or not an animal is experiencing kidney transplant rejection. There is no resolution as to how detecting phosphorylated SEQ ID NO:1 relates to the method and the disease. The minimum requirements for method steps minimally include a contacting step in which the reaction of the sample with the reagents necessary for the assay is recited, a detection step in which the reaction steps are quantified or visualized, and a correlation step describing how the results of the assay allow for the determination.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 2, 9 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: a method of monitoring whether an animal that has received a transplanted kidney is experiencing kidney transplant rejection, the method comprising: analyzing a sample of the kidney of the animal for the presence of a marker protein selected from the group consisting of: (a) phosphorylated protein which is SEQ:ID NO. 1 in a form comprising phosphorylated tyrosine; and (b) protein which is SEQ: ID NO. 1; wherein the

analyzing comprises: contacting the sample or a homogenate thereof with **a labeled antibody that specifically binds to SEQ ID NO:1**; detecting the extent to which labeled antibody becomes bound to the marker protein or said fragment as a result thereof; and either: (i) comparing the amount of marker protein bound to the labeled antibody to a known standard to diagnose whether the animal is experiencing kidney transplant rejection, whereby the method is conducted such that if no such marker protein is thereby detected in the sample, or if the amount of marker protein thereby detected in the sample is below a known standard level, such a result would be indicative of kidney transplant rejection; or (ii) comparing the amount of said fragment bound to the labeled antibody to a known standard to diagnose whether the animal is experiencing kidney transplant rejection, whereby the method is conducted such that if no such fragment bound to the labeled antibody is thereby detected, or if the amount of such fragment bound to the labeled antibody thereby detected is below a known standard level, such a result would be indicative of kidney transplant rejection of claim 17; wherein the animal is a primate of claim 2; and wherein the animal is a human of claim 9; does not reasonably provide **enablement** for: a method of monitoring whether an animal that has received a transplanted kidney is experiencing kidney transplant rejection, the method comprising: analyzing a sample of the kidney of the animal for the presence of a marker protein selected from the group consisting of: (a) phosphorylated protein which is SEQ:ID NO. 1 in a form comprising phosphorylated tyrosine; and (b) protein which is SEQ: ID NO. 1; wherein the analyzing comprises: contacting the sample or a homogenate thereof with **a labeled antibody capable of binding to the marker protein in the sample, or to a fragment of the marker protein** in the homogenate; detecting the extent to which labeled antibody becomes bound to the marker protein or said fragment as a

result thereof; and either: (i) comparing the amount of marker protein bound to the labeled antibody to a known standard to diagnose whether the animal is experiencing kidney transplant rejection, whereby the method is conducted such that if no such marker protein is thereby detected in the sample, or if the amount of marker protein thereby detected in the sample is below a known standard level, such a result would be indicative of kidney transplant rejection; or (ii) comparing the amount of said fragment bound to the labeled antibody to a known standard to diagnose whether the animal is experiencing kidney transplant rejection, whereby the method is conducted such that if no such fragment bound to the labeled antibody is thereby detected, or if the amount of such fragment bound to the labeled antibody thereby detected is below a known standard level, such a result would be indicative of kidney transplant rejection of claim 17; wherein the animal is a primate of claim 2; and wherein the animal is a human of claim 9. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in

the art to practice the claimed invention.

On pages 7-20 of the specification a method is disclosed for analyzing kidney tissue samples for the phosphorylated protein of SEQ ID NO:1 to determine kidney transplant rejection status. Experiments were performed by immunoblot using of anti- phosphotyrosine antibody after SDS-PAGE 2 D gel electrophoresis, polyacrylamide electrophoresis, mass spectrometry, immunohistochemistry, light microscopy and RT-PCR from kidney tissue samples of mice, rhesus monkeys, baboons and rats.

The specification does not adequately disclose a method of monitoring whether an animal is experiencing kidney transplant rejection using an antibody that specifically binds to any other protein or peptide than the protein of SEQ ID NO:1. As recited, the claims encompass using an antibody that binds to any 2 or more amino acid subsequence of SEQ ID NO:1 for use in the claimed method, though many of the encompassed peptides cannot bind even antibodies, much less monitor kidney transplant rejection. Without direction and guidance in the specification as to which antibodies specific for subsequence peptides would work in the claimed invention, such as guidance regarding requisite size and sequence of the peptides, it would require undue experimentation by one of ordinary skill in the art to practice the claimed invention commensurate in scope with the claims.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working

examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

12. Claims 2, 9 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of: A method of monitoring whether an animal that has received a transplanted kidney is experiencing kidney transplant rejection, the method comprising: analyzing a sample of the kidney of the animal for the presence of a marker protein selected from the group consisting of: (a) phosphorylated protein which is SEQ:ID NO. 1 in a form comprising phosphorylated tyrosine; and (b) protein which is SEQ: ID NO. 1; wherein the analyzing comprises: contacting the sample or a homogenate thereof with **a labeled antibody that specifically binds to SEQ ID NO:1**; detecting the extent to which labeled antibody becomes bound to the marker protein or said fragment as a result thereof; and either: (i) comparing the amount of marker protein bound to the labeled antibody to a known standard to diagnose whether the animal is experiencing kidney transplant rejection, whereby the method is conducted such that if no such marker protein is thereby detected in the sample, or if the amount of marker protein thereby detected in the sample is below a known standard level, such a result would be indicative of kidney transplant rejection; or (ii) comparing the amount of said fragment bound to the labeled antibody to a known standard to diagnose whether the animal is experiencing kidney transplant rejection, whereby the method is conducted such that if no such

fragment bound to the labeled antibody is thereby detected, or if the amount of such fragment bound to the labeled antibody thereby detected is below a known standard level, such a result would be indicative of kidney transplant rejection of claim 17; wherein the animal is a primate of claim 2; and wherein the animal is a human of claim 9.

Applicant is not in possession of: a method of monitoring whether an animal that has received a transplanted kidney is experiencing kidney transplant rejection, the method comprising: analyzing a sample of the kidney of the animal for the presence of a marker protein selected from the group consisting of: (a) phosphorylated protein which is SEQ:ID NO. 1 in a form comprising phosphorylated tyrosine; and (b) protein which is SEQ: ID NO. 1; wherein the analyzing comprises: contacting the sample or a homogenate thereof with **a labeled antibody capable of binding to the marker protein in the sample, or to a fragment of the marker protein** in the homogenate; detecting the extent to which labeled antibody becomes bound to the marker protein or said fragment as a result thereof; and either: (i) comparing the amount of marker protein bound to the labeled antibody to a known standard to diagnose whether the animal is experiencing kidney transplant rejection, whereby the method is conducted such that if no such marker protein is thereby detected in the sample, or if the amount of marker protein thereby detected in the sample is below a known standard level, such a result would be indicative of kidney transplant rejection; or (ii) comparing the amount of said fragment bound to the labeled antibody to a known standard to diagnose whether the animal is experiencing kidney transplant rejection, whereby the method is conducted such that if no such fragment bound to the labeled antibody is thereby detected, or if the amount of such fragment bound to the labeled

antibody thereby detected is below a known standard level, such a result would be indicative of kidney transplant rejection of claim 17; wherein the animal is a primate of claim 2; and wherein the animal is a human of claim 9.

The specification discloses an antibody that specifically binds to SEQ ID NO:1 for use in the claimed method. There is a lack of written description in the specification for the use of antibodies that may bind any 2 or more amino acid subsequence of SEQ ID NO:1 in the claimed invention, as encompassed by the instant claims. The specification further does not describe the requisite structure or size for a protein fragment which an antibody could specifically bind to monitor kidney transplant rejection.

Applicant has disclosed only a method of monitoring whether an animal is rejecting a transplanted kidney using an antibody that specifically binds to SEQ ID NO:1; therefore, the skilled artisan cannot envision all the contemplated antibody possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method.

Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description"

Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

August 3, 2007

Nora M. Rooney, M.S., J.D.

Patent Examiner

Technology Center 1600

Maher M. Haddad

MAHER M. HADDAD
PRIMARY EXAMINER